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Gene therapy: some results, many problems to solve.

Fischer A.

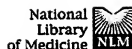
INSERM Unit 429, Hôpital Necker-Enfants Malades, Paris, France. fischer@necker.fr

Gene therapy is raising incredible hopes. The prospects of treating numbers of severe pathologies (hereditary, cancerous, degenerative or infectious) are vast. Nevertheless, the technological bolts to lift are still numerous, whether they be bringing the vectors into focus, the systems of expression of transgenes or the neutralization of immune responses of the host against the vector, the product of transgenes, or the knowledge of the considered pathologies of physiopathology. Solving these difficulties entails the gathering of multiple disciplines, from chemistry to medicine, passing through virology and immunology.

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Nippon Geka Gakkai Zasshi. 2001 Oct;102(10):778-82. Japanese.
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☐ 11: [No authors listed]

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Liver-directed gene therapy: promises, problems and prospects at the turn of the century.
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Mar 20, 2003

DOCUMENT-IDENTIFIER: US 20030054009 A1

TITLE: Clostridium difficile vaccine

CLAIMS:

3. A vaccine as claimed in claim 1 or 2 wherein the gene encodes a C. difficile surface layer protein, SlpA or variant or homologue thereof.

4. A vaccine as claimed in claim 1 or 2 wherein the peptide/polypeptide is a C. difficile surface layer protein, SlpA or variant or homologue thereof.

6. A vaccine as claimed in 5 wherein the chimeric nucleic acid sequence is derived from the 5' end of the gene, encoding the mature N-terminal moiety of SlpA from C. difficile.

8. A vaccine as claimed in 7 wherein the amino acid sequence of the chimeric peptide/polypeptide is derived from the mature N-terminal moiety of SlpA from C. difficile.

20. A vaccine for the treatment or prophylaxis of C. difficile associated disease, the vaccine comprising the mature N-terminal moiety of a surface layer protein, SlpA of C. difficile or variant or homologue thereof which is immunogenic in humans.

21. A vaccine as claimed in claim 20 wherein the N-terminal moiety of SlpA contains an amino acid sequence SEQ ID No. 1.

22. A vaccine as claimed in claim 20 wherein the N-terminal moiety of SlpA contains an amino acid sequence SEQ ID No. 2.

40. A chimeric nucleic acid sequence derived from the 5' end of the slpA gene encoding the mature N-terminal moiety of SlpA from C. difficile which is immunogenic in humans.

41. A chimeric peptide/polypeptide wherein the amino acid sequence of the chimeric peptide/polypeptide is derived from the mature N-terminal moiety of SlpA from C. difficile.

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Primary accession number Q9EY85
Secondary accession numbers None
Entered in TrEMBL in Release 16, March 2001
Sequence was last modified in Release 16, March 2001
Annotations were last modified in Release 24, June 2003

Name and origin of the protein

Protein name SlpA
Synonyms None
Gene name **Name:** slpA
From Clostridium difficile [TaxID: 1496]
Taxonomy Bacteria; Firmicutes; Clostridia; Clostridiales; Clostridiaceae; Clostridium.

References

[1] NUCLEOTIDE SEQUENCE.

STRAIN=79685;
DOI=10.1128/IAI.69.5.3442-3446.2001; PubMed=11292772 [NCBI, ExPASy, EBI, Israel, Japan]
Karjalainen T.K., Waligora-Dupriet A.J., Cerquetti M., Spigaglia P., Mauri P., Mastrantonio P.;
"Molecular and genomic analysis of two genes encoding surface-anchored proteins from
Clostridium difficile.";
Infect. Immun. 69:3442-3446(2001).

Comments

None

Cross-references

EMBLAY004256; AAF89093.1; -;
Genomic_DNA.

IPR007253; Cell_wall_bd_2.

[EMBL] GenBank / DDBJ
[CoDingSequence]**InterPro**

IPR002035; VWF_A.

Graphical view of domain structure.

Pfam

PF04122; CW_binding_2; 2.

Pfam graphical view of domain structure.

PRINTS

PR00453; VWFADOMAIN.

ProDom

[Domain structure / List of seq. sharing at least 1 domain]

HOGENOM

[Family / Alignment / Tree]

ProtoMap Q9EY85.
 PRESAGE Q9EY85.
 ModBase Q9EY85.
 SWISS-2DPAGE Get region on 2D PAGE.
 UniRef View cluster of proteins with at least 50% / 90% / 100% identity.

Keywords

None

Features

None

Sequence information

Length: 717 Molecular weight: 76398 CRC64: 52EA6146034FE36B [This is a checksum on the
 AA Da sequence]

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70	80	90	100	110	120
YNYKSDATTA	DAKEIAATTL	YNLVDSKLDN	LGDGDLVSFN	IKYDAAEKPH	TKDEMDALKT
130	140	150	160	170	180
KLENKEIVKP	ASETAGLVLM	ADGATDSKKA	DKSLYAKDVI	KFDVVSDTIG	YKLTATPIAD
190	200	210	220	230	240
AQLATLKATY	KYANNTKVEF	ASATELAATD	GSAVEVAKGK	EYNATGSLVF	DSATGKTSNI
250	260	270	280	290	300
NVDPLTNKGD	TVVKVINAKE	STIDIDSSTS	TSAEDLAKKY	VFDEDKLDDI	YKELTSEEGY
310	320	330	340	350	360
GNLVQLVSGR	YQVALYPEGK	RLDTKGATDI	ENTPVKLVLK	ADKIKDMKDY	IDDLRTYNNS
370	380	390	400	410	420
YSNVVTVAGE	DRIETAIELS	NKYNSDDKH	AITDSATDSV	VLVGSQAIVD	GLVASPLASE
430	440	450	460	470	480
KHAPLLLTSK	DKLDSNVKSE	IKRVMDLKST	SGINTSKKVY	LAGGVNSISK	EVENELKDMG
490	500	510	520	530	540
LKVTRLSGDD	RYETSLAIAD	EVGLDNDKAF	VVGGTGLADA	MSIAPVASQL	KKSNGDLDDV
550	560	570	580	590	600
DGDATPIVVV	DGKARTINNE	TEDFLNNAQV	DIIGGENSVS	KDVEKSIIVA	TGKEPNRTSG
610	620	630	640	650	660
DDRQATNAEV	MKETDYFEKG	SVINYFVAKD	GSTKEDQLVD	ALAAAPVAAN	FGSTYDGKNA
670	680	690	700	710	
NGTVSPAPIV	LATDSLADQ	NVGVSXSVD	DGGKNLVQVG	KGIASSVISK	MKDLLDM

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[\[Features\]](#) [\[Sequence\]](#) [\[Tools\]](#)

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Entry information

Entry name	SLAP2_THET8
Primary accession number	P35830
Secondary accession number	Q6LCW2
Entered in Swiss-Prot in	Release 29, June 1994
Sequence was last modified in	Release 29, June 1994
Annotations were last modified in	Release 49, January 2006

Name and origin of the protein

Protein name	S-layer protein [Precursor]
Synonyms	P100 protein Surface layer protein

Gene name	Name: slpA
	Synonyms: slb

From	Thermus thermophilus (strain HB8 / ATCC 27634 / [TaxID: 300852]) DSM 579)
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Taxonomy	Bacteria; Deinococcus-Thermus; Deinococci; Thermales; Thermaceae; Thermus.
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References

- [1] NUCLEOTIDE SEQUENCE [GENOMIC DNA].
PubMed=1429468 [NCBI, ExPASy, EBI, Israel, Japan]
Faraldo M.M., de Pedro M.A., Berenguer J.;
"Sequence of the S-layer gene of Thermus thermophilus HB8 and functionality of its promoter in Escherichia coli."; J. Bacteriol. 174:7458-7462(1992).
- [2] NUCLEOTIDE SEQUENCE [GENOMIC DNA] OF 1-11.
PubMed=7476196 [NCBI, ExPASy, EBI, Israel, Japan]
Fernandez-Herrero L.A., Badet-Denisot M.-A., Badet B., Berenguer J.;
"glmS of Thermus thermophilus HB8: an essential gene for cell-wall synthesis identified immediately upstream of the S-layer gene."; Mol. Microbiol. 17:1-12(1995).

Comments

- **FUNCTION:** The S-layer is a paracrystalline mono-layered assembly of proteins which coat the surface of bacteria.
- **SUBUNIT:** Forms trimers in the presence of calcium.
- **SUBCELLULAR LOCATION:** Cell wall. This bacterium is covered by a S-layer with hexagonal symmetry.
- **SIMILARITY:** Contains 1 SLH (S-layer homology) domain.

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Cross-references

EMBL	X57333; CAA40609.1; -;	[EMBL / GenBank / DDBJ]
	Genomic_DNA.	[CoDingSequence]
	U17352; AAA86987.1; -;	[EMBL / GenBank / DDBJ]
	Genomic_DNA.	[CoDingSequence]
PIR	S26365; S26365.	
InterPro	IPR001119; SLH.	
	Graphical view of domain structure.	
Pfam	PF00395; SLH; 1.	
	Pfam graphical view of domain structure.	
PROSITE	PS01072; SLH_DOMAIN; 1.	
ProDom	[Domain structure / List of seq. sharing at least 1 domain]	
HOGENOM	[Family / Alignment / Tree]	
BLOCKS	P35830.	
ProtoNet	P35830.	
ProtoMap	P35830.	
PRESAGE	P35830.	
DIP	P35830.	
ModBase	P35830.	
SWISS-2DPAGE	Get region on 2D PAGE.	
UniRef	View cluster of proteins with at least 50% / 90% / 100% identity.	

Keywords

Cell wall; S-layer; Signal.

Features



Feature table viewer



Feature aligner

Key	From	To	Length	Description	FTId
SIGNAL	1	23	23	Potential.	
CHAIN	24	917	894	S-layer protein. PRO_0000032641	
DOMAIN	24	86	63	SLH.	

Sequence information

Length: 917 AA [This is the length of the unprocessed precursor]

Molecular weight: 96133 Da
[This is the MW of the unprocessed precursor]

CRC64: 16175929CF4CB78F [This is a checksum on the sequence]

<u>10</u>	<u>20</u>	<u>30</u>	<u>40</u>	<u>50</u>	<u>60</u>
MKKRLVTLTA	GLLTVLSMGF	GLAQFSDVPA	GHWAKEAVEA	LAAGKIILGF	PDGTFRGNN
<u>70</u>	<u>80</u>	<u>90</u>	<u>100</u>	<u>110</u>	<u>120</u>
LTRYQAAILI	YRLQLQIBEE	LKTQGTSPMT	EALAPEDLEA	MIAELKAQPM	PEPGMDQAAL
<u>130</u>	<u>140</u>	<u>150</u>	<u>160</u>	<u>170</u>	<u>180</u>
KDLMDRVEAA	SIAADTALAQ	AQQLAERLDA	LAQDVEGVKG	DLAGLSRQVE	ANADAIQALN
<u>190</u>	<u>200</u>	<u>210</u>	<u>220</u>	<u>230</u>	<u>240</u>


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ELAVLLNQDV LSLQDRVTAL EKMVSGGQEL PDLEQFATKE DVAAVQEFAA ALRSDLVGLS
      250      260      270      280      290      300
EKVSKLEGTV GDLSGKVATL QRNAPTISGS LSLNYSVYRA WGPDASAAGP GTANTPDIDR
      310      320      330      340      350      360
LFSSKFSFGD GNGNGSVGDE ADLGKNTGTV TNATLSVSFS TGKLDAAADP GKLNSYPGLV
      370      380      390      400      410      420
QFSRLAKLTN PGKYDPSTGA PTYPINLTLD EFSSTLAVAK DQTLSPFSGR SVRSKPTTEV
      430      440      450      460      470      480
FDNDYNSRGH GFVATYKPGI LGATLTGVYG SKGANNGDFT YFRGARLALS PVEGIALGGS
      490      500      510      520      530      540
FVQEGLDANQ GTTSASFAP TTVYGVDAKV KLGPVGLAGE YFNDAAPNA NGYVVKADVA
      550      560      570      580      590      600
LGSISVAGNY RNIGAGVTGA NMLSGDATST LDQGGWGGVD SSGNVINGAP FRSNRQGFGV
      610      620      630      640      650      660
SASAGLGPIT VKGYDSSSTV LANETITNSY GAFNYSANNQ LVAYGGQADL AFGGFTLSGF
      670      680      690      700      710      720
YRIAQLNGST TRYILTEKPA EAVYASEYGA KLAHDGASKD ALVPKLNFTA AYTKQYDNAT
      730      740      750      760      770      780
SGFTTQDIIV YGSYELALGP LTLKPMGRYH TQDAAAASST SDYTTVKYGV AASIALDLFP
      790      800      810      820      830      840
KPSLSGEYYA RSTQVTSANS GSSATGTISE SKYAVGLKLG EFLFKNSSVE AKYASYTGSG
      850      860      870      880      890      900
LNAPILLGVA DAASSTTSDY LYNNVAVSVG SNRGSVTGWY FTWTYNDLTF AYVEADVNNN
      910
GNQTHGQAFK ISYTVKF

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P35830 in FASTA
format

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BLAST

BLAST submission on
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Sequence analysis tools: ProtParam, ProtScale,
Compute pI/Mw, PeptideMass, PeptideCutter,
Dotlet (Java)



ScanProsite, MotifScan



Submit a homology modeling request to SWISS-
MODEL

NPSA

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tools



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L5: Entry 3 of 7

File: EPAB

Oct 14, 1999

DOCUMENT-IDENTIFIER: WO 9951631 A1

TITLE: A PROTEIN REGION RESPONSIBLE OF BINDING TO EPITHELIAL CELL TYPES AND A DNA SEQUENCE ENCODING SAID REGION

Abstract Text (1):

CHG DATE=19991102 STATUS=O>This invention relates to a DNA molecule encoding a polypeptide responsible of binding to human and/or animal epithelial cell types. It has been found that various fragments of S-layer protein SlpA of Lactobacillus brevis has adhesive properties to epithelial cells types. It is possible to modify or improve the binding capacity of various prokaryotic or eucaryotic cells to human and/or animal epithelial cell types, like intestinal, urogenital and/or endothelial cell types by using lactobacillar surface structures of this invention. In particular, it is possible with the nucleotide sequences of this invention to improve the binding properties of a host cell having probiotic effects to human and/or animal epithelial cell types.

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	#14 Search slpa gene Sort by: PublicationDate	09:33:12	4
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